PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of

Keiichi KAWAI, et al.

Appln. No.: 10/018,745

Confirmation No.: 2602

Filed: December 21, 2001

Docket No: Q67507

Group Art Unit: 1616

Examiner: Dameron L. JONES

For: METHOD OF THE ADMINISTRATION OF DRUGS WITH BINDING AFFINITY FOR PLASMA PROTEIN AND PREPARATION TO BE USED IN THE METHOD

REPLY BRIEF PURSUANT TO 37 C.F.R. § 41.41

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the provisions of 37 C.F.R. § 41.41, Appellant respectfully submits this Reply Brief in response to the Examiner's Answer dated November 26, 2004. Entry of this Reply Brief is respectfully requested.

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STATUS OF AMENDMENTS

In item (4), on page 2 of the Examiner's Answer, the Examiner states that appellants' statement in the Brief of the status of the amendment after final rejection is not correct.

In particular, the Examiner states that the amendment after final rejection was entered. In Section IV, at page 2 of the Brief, appellant stated that the Examiner indicated in an Advisory Action dated June 21, 2004 that the amendment after final would be entered.

Accordingly, appellant does not understand why the Examiner considers appellants' statement of the status of the amendment after final rejection to be incorrect.

In any event, since appellants and the Examiner both agree that the amendment after final was entered, and since the Examiner has separately indicated in items (3) and (8) of the Examiner's Answer that the statement of the status of the claims and the copy of the appealed claims in the Appendix are correct, appellants believe that no further action is required.

SUMMARY OF THE INVENTION

In item (5) of the Examiner's Answer, the Examiner states that appellants' summary of independent claim 21 in the Brief is not consistent with pending claim 21 because independent claim 21 identifies verapamil as the second drug, whereas the summary does not refer to verapamil. Appellants confirm that the summary of independent claim 21 should be understood as having verapamil as the second drug. See page 6, lines 4 to 9 of the specification for a disclosure of verapamil as the second drug.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following two grounds of rejection, set forth in item (10) of the Examiner's Answer, are to be reviewed on appeal.

(a) Claims 1 to 17, 21, 23 and 25 have been rejected as being anticipated by Somogyi et al.

Appellants note that claims 1 to 13 have been canceled. Accordingly, appellants believe that this rejection is applicable to claims 14 to 17, 21, 23 and 25.

(b) Claims 14, 16 to 19 and 21 to 27 as obvious over Somogyi et al in view of Li et al.

ARGUMENT

(a) The Rejection of Claims 1 to 17, 21, 23 and 25 as being Anticipated by Somogyi et al.

As noted above, appellants believe that the Examiners' statement of this rejection is not correct because claims 1 to 13 have been canceled.

Appellants submit that the main Brief adequately addresses various points that the Examiner has raised. Appellants set forth the following additional arguments.

(i) The Examiner states at page 7, last paragraph, that "it would be inherent that if you have two forms of the same drug that desire the same binding site wherein the drugs are co-administered, then there will be a competing for the binding site". The Examiner makes a somewhat similar statement at page 8, lines 7 to 10. The Examiner apparently believes that if there is competing at a binding site, then the binding will be regulated.

Appellants disagree with the Examiner's statements.

In particular, appellants point out that regulation of binding will occur only if one drug or one form of drug has a different binding affinity than another drug. The Examiner has not provided any evidence that the different drugs or drug forms in Somogyi et al have different binding affinity.

Appellants submit that plasma protein binding is not affected by the use of two different forms of the same drug such as verapamil. Thus, when the active ingredient of the drugs to be administered is the same, binding affinity of the active ingredient for plasma protein can not be regulated, even though the drugs have different forms or are administered by different routes (oral, intravenous, etc.). Regulation of plasma protein binding can be done with two different

drugs (active ingredients) when the second drug has binding affinity for the same plasma protein for which the first drug has binding affinity, i.e., a first drug and a second drug that is different from the first drug, as in the present invention.

Further, Somogyi et al state at page 52, 2nd column, next to last paragraph, that binding was determined at four different concentrations, 10, 25, 50 and 100 mg/ml plasma, and further state at page 55, first column that "the free fraction of verapamil in plasma...[in percentage terms] was independent of the total verapamil concentration".

This indicates that the binding was the same, regardless of the verapamil concentration.

Since the discussion at page 55, first column, relates to the simultaneous use of two different forms of verapamil, this can be an indication that the plasma binding was not affected by the use of the two different forms, and that one form did not regulate the binding of the other form.

In summary, the regulation of plasma binding is not inherent in the various drug combinations that the Examiner has referred to.

(ii) The Examiner also refers to Figures 1 and 2 at page 55 for support of his argument that Somogyi et al disclose regulation of plasma binding.

Appellants submit that Figures 1 and 2 of Somogyi et al do not in any way show regulation of plasma binding.

Figure 2 relates to the % increase in P-R interval as a function of time in patients with a liver cirrhosis and in a normal subject. However, the change in P-R time interval with time is an ECG effect (heart function value), and has nothing to do with plasma binding.

Further, with respect to Figure 1, it shows the plasma concentrations of verapamil as a function of time following intravenous administration of 10 mg verapamil (a) and oral administration (b) of 40 mg d_3-verapamil in a patient with liver cirrhosis and 80 mg d_3-verapamil in a normal subject.

The discussion in (i) above applies to Figure 1.

Thus, Figure 1 does not show binding regulation by the use of the two different forms of verapamil.

(iii) Appellants further note that claims 15 and 22 recite that the second drug has binding affinity to the same binding sites on plasma protein to which the first drug has binding affinity. Somogyi et al do not contain any discussion of binding sites on the plasma protein.

(b) <u>The Rejection of Claims 14, 16 to 19 and 21 to 27 as Obvious over Somogyi et al in view of Li et al.</u>

The Examiner relies on Li et al to show the use of a kit comprising first and second drugs and other possible radiolabels and/or chelators that may be used to radiolabel drugs.

Appellants submit that the main Brief adequately addresses all of the points raised by the Examiner.

Further, appellants submit that the Examiner's reliance on Li et al is based on hindsight. There is no teaching in Li et al that would lead one to select verapamil from the list provide in Li et al, and combine it with a drug whose plasma binding would be regulated by the verapamil. Since Li et al do not disclose an example of the use of verapamil with another specific drug, it would be hindsight to select another drug whose plasma binding was regulated by verapamil.

CONCLUSION

For the above reasons as well as the reasons set forth in Appeal Brief, appellants respectfully request that the Board reverse the Examiner's rejections of all claims on appeal. An early and favorable decision on the merits of this appeal is respectfully requested.

Respectfully submitted,

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